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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WESSENDORF, TERESA D	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 09/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/842,873	KOGANTY ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,16,17,19-31 and 42-53* is/are pending in the application.

4a) Of the above claim(s) *16,24,25 and 28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,17,19-23,26,27 and 42-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/1/2005 has been entered.

Election/Restrictions

Applicants asked for clarification of the status of claim 30. Applicants state that the office action mailed December 17, 2003 listed the claim as withdrawn. The present action did not explicitly rejoin claim 30 as it did claim 23 (see page 3 of OA), but claim 30 is listed as rejected in the office action summary, and as "under examination" on page 4. Hence, we have treated it as no longer withdrawn.

In response, a review of claim 30 would indicate that this claim is drawn to a method wherein the carbohydrate structures are associated with a human cell surface antigen acting as a receptor for a bacterial adhesion ligand. Hence, this claim is

drawn to a different species, as stated at page 4, paragraph one of the Office action and has been withdrawn from examination. The inadvertent inclusion of said claim in the status of the claims and the Summary action (PTO-326) is regretted.
To clarify the status of claim 30, the claim is withdrawn from examination, as being drawn to the non-elected species.

Status of Claims

Claims 1-11, 16-17, 19-31 and 42-53 are pending in the application.

Claims 12-15, 18, 32-41 have been cancelled.

Claims 16, 24-25 and 28-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species.

Claims 1-11, 17, 19-23, 26-27 and 42-53 are under examination.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 17, 19-23, 26-27 and 42-53, as amended, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons set forth in the last Office action, 1/14/2005.

Response to Arguments

A. Applicants argue that previously, claim 1 explicitly taught randomly glycosylating a "platform" (i.e., a peptide) to obtain a first level library. That step clearly provided a first level library. We chose to amend the claim to emphasize the creation of second and higher level libraries. Claims 43 and 44 address how the first level library was provided.

In response, while the previous claim 1 recites positive, manipulative process step i.e., of glycosylating randomly a peptide however, providing is not a positive, manipulative step of the process. The as-filed specification does not recite or define a "providing" step. Providing can be interpreted as from

a commercial source or other sources instead of being generated by applicants. It is not seen as to the essentiality of the "providing" step (when the synthesis commences with he glycosylation of the peptide. [The original claim 1 presents a clearer claim except for the term "platform".]

It is stated that page 9, lines 10-12 provides basis for a claim to a method of making a second level library from a first level library, without explicitly reciting the first level synthesis in the claim. The examiner does not explicitly point out what is wrong with claims 42-53, added June 17, 2004. It is difficult, of course, to defend limitations not specifically attacked.

In reply, it is indeed difficult to specifically point out whether the amendments made in the claims are in the as-filed specification since the amendments are too numerous to mention specifically. [Applicants have again not pointed out support for the present amendments in the as-filed specification.] MPEP 714.02 states that it is incumbent upon applicants to point out where in the specification support for the numerous amendments in the claims can be found. Applicants point out the support for newly added claims 42-53. Except for claim 42, the other claims find support in the as-filed specification. Support for claim 42 is stated as found at page 9, lines 5-7. A review of this

section does not provide support for the limitations in claim 42 that all the glycopeptides in step (a) is identical. Furthermore, while support for claims 42-53 has been given, support for the other amended claims have not been provided. For example, claim 11, some, but not all; claim 17 "the identify of the amino acid …."

The presently amended claims, which are not supported in the as-filed specification, are as follows:

Claim 1 drawn to a library comprising a ***plurality*** of library members…including glycopeptides comprising at least one ***carbohydrate*** structure comprising a least two sugar units. The as-filed specification does not recite for a "plurality". It is considered that since a library is composed already of several members, then the members are in plurality, unless otherwise intended. [Then the term "plurality" is redundant. This makes claim 1 confusing as to what is actually intended or claim.] It seems that the claims recite for what is more than disclosed in the original specification which is a library. Furthermore, carbohydrate structure comprising at least two sugar units is broader than the original disclosure. The claims imply a whole carbohydrate unit, which contains at least two sugar units, rather than the specific sugar units in the as-filed specification.

A1). To satisfy a written description requirement for a claimed genus a sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406. A representative number of species means that the species, which are adequately described, are representative of the entire genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure indicates that the applicants have invented species sufficient to constitute the gen[us]. Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004).

The specification describes a species, MUC1, Seq. ID. 1, glycosylated by specific glycosyl unit. This single species would not provide as an adequate description for the huge scope of the genus claimed core peptide and carbohydrate structures with at least two sugar units. There is no correlation made in the specification as to the structures of the genus claims that

correlate to the single species recited in the specification. The genus claim does not recite any structure consequently; it is hard to establish its synthesis. It is well known in the art that oligosaccharides, let alone, carbohydrates are very complex and diverse, that makes the synthesis complex. The issues of stereochemistry at the anomeric position and the multiple hydroxyl groups present complicate it. A written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name of the claimed subject matter sufficient to distinguish it from other materials. University of California v. Eli Lilly and Col, 43 USPQ 2d 1398, 1405(1997), quoting Fiers V. Revel, 25 USPQ 2d 1601m 16106 (Fed. Cir. 1993). In biotechnological invention one cannot necessarily claim a genus after only describing a single species because there may be unpredictability in the results obtained from species other than those specifically described. The more unpredictable the art the greater the showing required (e.g. by (representative examples) adequate disclosure.

B. Claims 1-11, 17, 19-23, 26-27 and 42-53, as amended, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for mucin 1(MUC1) as the platform and inhibitory activity for a compound in the library,

does not reasonably provide enablement for the broadly recited combinatorially-generated library of glycopeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons advanced in the last Office action 1/14/2005.

Response to Arguments

Applicants state that claim 1 has been amended to recite MUCI, or a fragment thereof, as the "core peptide". Applicants state that the Examiner concedes that the specification is enabling for "mucin 1 (MUCI) as the platform". Applicants state that the issue of fragments of MUCI is not specifically addressed. Two MUCI fragments, SEQ ID NO:1 (16 a.a., claim 3) and SEQ ID NO:2 (4 a.a., claim 4) are specifically claimed. It is within ordinary skill in the art to identify a fragment of MUCI which contains one or more O-glycosylation and/or N-glycosylation sites as taught at P6, L14-20. It is clear from P12, L3 that the contemplated fragments may be as small as a tetrapeptide.

In reply, the Office action at page 10, paragraph specifically states Seq. ID. 1 as being enabled. It is not seen how a tetrapeptide, which is already a small fragment, can still be fragmented into smaller peptides. The tetrapeptide contains

only one Ser(OH) for glycosylation and it is not seen the "more" than one residue that is glycosylated.

Claim Rejections - 35 USC § 112, second paragraph

In view of the amendments and arguments to claims 46-47, the rejection of these claims in the last office action is withdrawn. However, the following rejections, as applied to the amended claims are as follows:

Claims 1-11, 17, 19-23, 26-27 and 42-53, as amended, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1, for example, is being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: the peptide and carbohydrate units. It is not clear how synthesis can occur given no structure for each of the compound or moiety involve in the synthesis reaction.

B. Claim 9 is unclear as to which glycopeptides is being referred to as the base claim does not recite for a hydroxyl

groups or glycosyl donor. This rejection has similar import to claims 10-11 as to the hydroxyl glycosylation.

C. Claim 11 is unclear as to the phrase "some but not all" as some is a relative term. This term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the genus invention.

D. Claim 20 is unclear as to the number and site of hydroxylysine or asparagines for the unglycosylated peptide, MUCI as recited in the base claim. The MUCI recited in the base claim, absent any structure, is unclear as to the hydroxyllys site, inter alia.

E. Claim 27 is unclear as to the spacing of the glycosylation sites in the unglycosylated peptides in clusters especially in the absence of definition in the specification as to what constitutes a cluster.

F. The limitations in claims 46 and 47 are already in the base claim except worded or rearranged differently. Applicants are simply multiplying the claims without adding any dependent limitations that is already present in the base claim.

G. It is not clear as to how the core peptide is derived from MUC1 core protein or from a cancer-associated mucin. E.g., claim 49 and 50.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 5-11, 17, 19-20, 22-23, 26=27 and 42-53, as amended, are rejected under 35 U.S.C. 103 as being obvious over Vetter et al (WO 95/18971) or Schleyer et al (Angew. Chem. Int.) in view of either Garg et al (Advanced in Carbohydrate Chemistry and biochemistry) or Arya (Angew. Chem. Int. Ed. Eng.) and Ding et al (Cancer Immunology Immunotherapy).

Vetter discloses at page 25, line 33 up to page 27, line 10 a method of generating a glycopeptide library of structure Ac-X-X-E (OA)XP-resin, X is any of the 18 side chain protected amino acids as recited therein. The peptide is coupled to a bead (a platform, as claimed). The sequence of reaction and random reapportionment continue until sequences having the desired lengths are formed. The glycosyl acceptor was produced by deprotecting and activating the side chain of Glu, which is

common to each of the molecules. A first set of glycosylating agents e.g., Gal Nac is introduced to the various aliquots of resin beads containing surface reactive functionality to yield a library of glycoconjugates. Aliquots of the original member library were diversified by conjugation to 17 different glycosylamines, inter alia, Gal Nac. See further page 5, summary up to page 7,line 27 and the Examples at pages 38-56. Vetter discloses or at least suggests at page 6, lines 15-25 the synthesis of linear glycoconjugates by repeating the steps of protecting, deprotecting and coupling.

Schleyer discloses at page 1976 a method for the generation of a multiple glycopeptides with variation of both sugar and peptide. Schleyer discloses that it is more efficient to couple the sugar directly and stereoselectively to the free hydroxyl groups of amino acid side chains on the resin-bound peptides. Thus, libraries of libraries could be produced by glycosylation of a preformed peptide library. See specifically the reaction schemes.

Each of Vetter or Schleyer does not disclose, a second glycosylation of the glycopeptide, albeit each at least suggests reiterative synthesis and Mucin, as claimed. However, Garg discloses at page 305 up to page 306, the lengthening of the glycopeptide through the sugar units. Garg discloses at page 277

that the synthesis of glycopeptide provides the purpose of supplying structurally well-defined derivatives as models for biochemical and immunochemical studies. Arya discloses at page 12, 81, col. 2 that random glycosylation of e.g., trisaccharides now make the synthesis of di- and trisaccharide combinatorial libraries a feasible process. This has a great impact in the understanding of cell-surface interactions and aid in the design of polyvalent compounds that inhibit these interactions.

Ding discloses the synthesis of the glycopeptide MUC1 at page 11, Fig. 1 with the sequence as shown therein. Ding further discloses at page 15 that the core peptide of MUC1 was chosen because of its strong association with human breast cancer and the fact that core peptide cryptic epitopes are revealed in cancer cells as a result of under glycosylation of mucin in carcinoma cells. Accordingly, it would have been obvious to one having ordinary skill in the art at the time the invention was made to glycosylate(i.e., lengthen, second level, as claimed) the glycopeptide (first level, as claimed) of either Vetter or Schleyer as taught by either Garg or Arya. Furthermore, to use mucin as the glycopeptide in the method of each of Schleyer or Vetter would be obvious at the time the invention was made as taught by Ding. The advantages in glycosylating a glycopeptide and using Mucin as the glycopeptide as taught by either Garg or

Arya and Ding would provide the motivation to one having ordinary skill in the art. The lengthening of the carbohydrate is known and conventionally done in the art. Thus, it would be within the ordinary skill in the art at the time the invention was made to lengthen the sugar units whether the sugar is by itself or coupled to a peptide. The same result of lengthening the sugar moiety is attained.

Applicants' arguments with respect to the 103 rejection over each o f Schleyer, Vetter and Ding is moot in view of the new grounds of rejection combined with the new found art.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is(571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T. D. Wessendorf

Primary Examiner

Art Unit 1639

Tdw

September 12, 2005